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The Lowly Diphtheroid: Nondiphtheria Corynebacterial Infections in Humans

These discussions are selected from the weekly staff conferences in the Department of Medicine, University of California, San Francisco. Taken from transcriptions, they are prepared by Drs. David W. Martin, Jr, Professor of Medicine, and James L. Naughton, Assistant Professor of Medicine, under the direction of Dr. Lloyd H. Smith, Jr, Professor of Medicine and Chairman of the Department of Medicine. Requests for reprints should be sent to the Department of Medicine, University of California, San Francisco, School of Medicine, San Francisco, CA 94143.

DR. SMITH:* *This Medical Staff Conference will be presented by Dr. Richard Locksley, a graduate of the University of California, San Francisco, medical residency program and former Chief Resident at the Moffitt Hospital. Rich is now a fellow in infectious diseases at the University of Washington. He will address the clinical spectrum of diseases caused by "the lowly diphtheroid."*

DR. LOCKSLEY:† Corynebacteria are Gram-positive, nonmotile, nonsporulating bacilli that often appear pleomorphic on Gram stain. The name, derived from Greek (*koryne* = club, *bakterion* = a little rod), refers to the characteristic club-shaped tapered appearance of *Corynebacterium diphtheriae* grown on Loeffler's media. Although human infection by *C diphtheriae* has been well described, this has not been true of the nondiphtherial corynebacteria. These organisms, usually designated "diphtheroids," are ubiquitous in the environment (soil, fresh and salt water); they are commensals of humans, animals and plants.[1]

Whereas the pathogenicity for animals of several of these *Corynebacterium* sp has been established,[2,3] their capacity for causing human infections has been infrequently reviewed.[4-7] There are several reasons:

First, there is still taxonomic confusion regarding the grouping and speciation of these organisms.[1] On the basis of cell-wall constituents, including mesodiaminopimelic and mycolic acids, corynebacteria are more closely related to the genera *Mycobacterium* and *Nocardia* than to other Gram-positive bacilli. Speciation is more problematic. Many laboratories do not identify *Corynebacterium* sp beyond excluding *C diphtheriae*. Several of these species can be frustratingly inactive biochemically if testing is done in the absence of serum- or lipid-supplemented media. Further, of 221 *Corynebacterium* strains isolated from burn patients, fully 90 percent remained unspeciated by criteria available in 1973.[8] The Centers for Disease Control (CDC) continue to organize unspeciated *Corynebacterium* into alphabetized groupings on the basis of fermentative and oxidative reactions. This foresighted approach has resulted in the recognition of the group JK organ-

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TABLE 1.—*Characteristics Differentiating Coryneform Bacteria That Cause Infection in Humans**

	Genera				
	Coryne-bacterium	*Listeria*	*Propioni-bacterium*	*Erysipe-lothrix*	*Kurthia*
Aerobe/facultative anaerobe	+	+	−	+	+
Motility	−	+ (21°C)	−	−	+ (35°C)
Catalase	+	+	+	−	+
Hemolysis on blood agar	Variable (β)	β	−	α	−
H_2S in triple sugar iron or Kligler iron agar	−	−	−	+	−

H_2S = hydrogen sulfide, + = positive, − = negative.

*Adapted from Lipsky et al.[7]

ABBREVIATIONS USED IN TEXT

CDC = Centers for Disease Control
CSF = cerebrospinal fluid
PVE = prosthetic valve endocarditis
SICU = surgical intensive care unit

isms as pathogens responsible for specific clinical syndromes.[9]

Second, because they are members of the normal flora, *Corynebacterium* sp are usually regarded as contaminants when they are isolated from clinical specimens. Diphtheroids grew from 10 percent and 16 percent of more than 30,000 blood cultures collected at the Mayo and Cleveland Clinics, respectively.[10,11] Whereas most of these isolates were insignificant, the preconception of diphtheroids as contaminants can lead to dire clinical consequences.

Third, some *Corynebacterium* sp require prolonged incubation or specialized growth conditions, or both. Isolations may be missed unless blind subcultures and stains are made from nonturbid blood culture media. In the analyses of blood culture isolates previously mentioned, the median time for detection of diphtheroids was nine days.[10,11] Pathogenic isolates may require similarly prolonged periods before detection.

Other bacteria causing human infection may appear coryneform on Gram stain and must be distinguished from *Corynebacterium* (Table 1). In the appropriate clinical setting (neonates, alcoholic patients, cerebrospinal fluid [CSF] specimens) "diphtheroid" isolates should be suspected of being *Listeria*. The rapidly growing mycobacteria, *Mycobacterium fortuitum* and *Mycobacterium chelonei,* may also stain as club-shaped Gram-positive bacilli. Other pleomorphic organisms that may be confused with *Corynebacterium* by Gram stain include *Actinomyces, Arachnia, Bacterionemia, Bifidobacterium, Eubacterium, Nocardia, Rothia* and *Streptomyces. Bacillus* sp are spore-forming.

Despite the difficulties in morphology and taxonomy, several distinctive clinical syndromes caused by some of the speciated diphtheroids have emerged. Although some of these observations are based on limited numbers of case reports, these cases are probably vastly underreported due to the difficulties previously enumerated. A comprehensive review, including historical and microbiological characteristics of these organisms, together with their pathogenicity for animals and humans, has recently appeared,[7] to which the reader is referred for information beyond the clinical reports summarized here.

The organisms are grouped according to their likely reservoir as a pathogen to humans (Table 2). They either are acquired after contact with animals (zoonosial) or are components of the endogenous flora. Some may be nosocomially acquired as well. It must be emphasized that these groupings are only probable; the true position of these organisms in the human ecosphere has been incompletely defined. Nevertheless, this organization may be clinically useful.

Zoonoses

Corynebacterium equi

C equi is primarily an animal pathogen. Suppurative bronchopneumonia (horses), cervical adenitis (pigs) and pyometra (cattle) have been described. The usual portal of entry is the respiratory tract. Organisms persist in contaminated soil.

There are eight reported cases in humans. The patients, four men and four women, ranged in age from 18 to 52 years.[12-18] Five of them reported exposure to animals, usually horses. All had severely compromised cell-mediated immunity; five had hematologic malignancy (two Hodgkin's, two other lymphoma, one acute lymphocytic leukemia), two were renal-transplant recipients and

TABLE 2.—*Sources of Nondiphtheriae Corynebacterial Infections in Humans and Their Probable Pathogens*

Zoonosially acquired
Corynebacterium equi
Corynebacterium ovis
(Corynebacterium pseudotuberculosis)
Corynebacterium ulcerans
Corynebacterium pyogenes
Corynebacterium bovis
Normal flora
Corynebacterium xerosis
Corynebacterium pseudodiphtheriticum
(Corynebacterium hofmannii)
Corynebacterium hemolyticum
? Group JK
Nosocomially acquired
Group JK
? *C xerosis*
? *C bovis*

one was receiving immunosuppressive therapy for plasma cell hepatitis. When tested, patients were anergic to skin tests and had normal immunoglobulin and leukocyte levels. Two had had splenectomy.

The eight cases presented with pneumonitis, frequently showing nodules on chest x-ray studies and usually occurring in the upper lobes (five/eight). Cavitation (five/eight) and empyema requiring chest tube drainage (two/eight) were complications. The diagnosis was established from cultures of specimens from lung biopsy (three), blood (three), bronchoscopic washings (four), pleural fluid (two), skin lesions (two) or nodes (one). The organism was rarely recovered in sputum (two/eight).

Two patients died of progressive infection; six were cured. One had surgical resection of a pulmonary lesion only. The other five all relapsed with pulmonary (four) or cutaneous lesions (two), or both, after receiving antibiotics for 10 to 20 days. Cure required prolonged antibiotic therapy. One patient, who relapsed with multiple subcutaneous abscesses and fistulae and a pharyngeal membrane—all of which grew *C equi*—was treated with erythromycin for six months.

Although *Corynebacterium parvum* (reclassified as *Propionibacterium acnes*) has been used to potentiate immunity in patients with malignancy, none of the patients who had hematologic malignancies had objective tumor responses during the course of their *C equi* infections.

C equi grows well on standard media, producing pink, mucoid colonies. It is frequently acid-fast. The organism has coccoid morphology on agar and bacillary forms in liquid media. It variably reduces nitrate and hydrolyzes urea but is inactive against carbohydrates. It is rarely isolated from normal human flora even among compromised hosts.[15]

Erythromycin and gentamicin are most active against *C equi* by in vitro susceptibility testing.[19] Therapy should be prolonged with erythromycin given orally after the acute illness has subsided.

C equi must be distinguished from other acid-fast organisms that can cause cavitating pneumonia in compromised hosts, including *Mycobacterium, Nocardia* and *Legionella micdadei.*

Corynebacterium ovis (Corynebacterium pseudotuberculosis)

Sheep are the most common animal reservoir for *C ovis,* which may cause suppurative lymphadenitis, skin abscesses and bronchopneumonia in these animals. Cattle and horses are also infected. Horse infections are prevalent in Nevada and California; the animals have hindfoot or truncal abscesses, usually in the late summer or fall.

The eleven reported human cases[20-28] occurred in previously healthy persons; ten of the patients were men. Seven cases occurred in Australia and two in the United States (Washington, California). Six had direct contact with sheep, four had contact with other farm animals and one consumed raw milk. The latter was the presumed source of infection because mammary gland infections have been described in cows.

Ten patients presented with localized lymphadenopathy (axilla, five; inguinal, three; cervical, two). Four were asymptomatic, but six noted systemic symptoms (fever, malaise) and a tender lymph node. Either surgical drainage or excision, or both, with administration of antibiotics, was required for cure. Persistent drainage and sinus tract formation recurred in five of ten cases, and reexcision and prolonged antibiotic therapy were necessary for recovery.

Pathologically, nodes were replaced by necrotizing granulomas. *C ovis* was grown from the tissue and usually visualized in the specimen by microscopy. The histologic appearance resembled tuberculous lymphadenitis, cat-scratch disease and lymphogranuloma venereum.

The 11th patient was a veterinary student working with horses who presented with a left lower lobe pneumonia and 31 percent eosinophilia.[21] A transbronchial biopsy showed all the features of eosinophilic pneumonia, but the specimen from

transtracheal aspiration grew a pure culture of *C ovis*. He recovered after a 14-day course of erythromycin. No other pulmonary pathogens could be implicated. The only other case that occurred in the United States (cervical adenitis) was also accompanied by eosinophilia (10 percent).[20]

C ovis grows slowly on blood agar (where it may be β-hemolytic) and best on Loeffler's media. Colonies can mimic *C diphtheriae* on Tindale's media, but *C ovis* is distinguished by its ability to hydrolyze urea. *C ovis* is closely related to both *C diphtheriae* and *Corynebacterium ulcerans*. All of these organisms are capable of phage-inducible diphtheria toxin production,[29] but no toxigenic strains of *C ovis* have been described from human cases. *C ovis* produces an exotoxin that causes dermonecrosis in animals.[30]

C ovis is sensitive to most antibiotics. Erythromycin, tetracyline and penicillin have been used successfully.

C ulcerans

C ulcerans is probably a commensal of horses and cattle. It can cause bovine mastitis and has been isolated from raw milk.

Most human isolates are pharyngeal and are generally from asymptomatic children living in rural areas. Only rarely is there an accompanying pharyngitis or tonsillitis.[31] Most reports are from England and describe typically sporadic cases among persons with a history of exposure to livestock or of raw milk ingestion.

C ulcerans can also produce phage-inducible diphtheria toxin, and occasional patients have presented with a full-blown diphtheria syndrome. Of 122 human strains evaluated in one series, 43 (35 percent) were toxigenic.[29] However, a diphtheria syndrome is rarely seen with *C ulcerans* infection, perhaps due to the lower levels of toxin produced by toxigenic strains as compared with *C diphtheriae*.[32] *C ulcerans* also produces a dermonecrotic exotoxin.[32]

The organisms grow best on Loeffler's or Tindale's media where the colonies resemble *C diphtheriae*. It is distinguished from *C diphtheriae* by its positive urease and inability to reduce nitrate and from *C ovis* by its ability to ferment starch.

Erythromycin is the therapeutic agent of choice. Diphtheria antitoxin may be administered in cases resulting from toxigenic strains.

Corynebacterium pyogenes

C pyogenes is a commensal and an occasional pathogen of cattle, sheep and pigs. It generally causes suppurative local infections but dissemination with metastatic abscesses has been described.[2,3] Infections in humans are uncommon and no characteristic clinical syndrome has emerged.[33-38] Endocarditis has been reported.[34]

C pyogenes shares with *Corynebacterium hemolyticum* several features that are atypical when compared with the other *Corynebacterium* sp. These two organisms are catalase negative and ferment lactose. Both are β-hemolytic on blood agar. Unlike *C hemolyticum, C pyogenes* does not show metachromatic granules after staining with alkaline methylene blue. *C pyogenes* produces a hemolysin and a dermonecrotic exotoxin.

Corynebacterium bovis

C bovis is a commensal of the bovine udder. The organisms can cause bovine mastitis and may contaminate milk.[2,3]

Only seven human cases have been reported[39,40]; a history of animal exposure was not obtained in most of these. Three cases had infections of the central nervous system (one meningitis, one epidural abscess with possible meningitis, one infected ventriculojugular shunt). A case of mastoiditis was also reported. The patient with the CSF shunt infection had hypocomplementemia and mesangiocapillary glomerulonephritis; *C bovis* antigen was seen in the glomeruli by immunofluorescence. Diphtheroids have been increasingly incriminated in cases of "shunt nephritis," but unfortunately speciation of these corynebacterial isolations has not been done.[41-43] Two cases of prosthetic valve endocarditis due to *C bovis* occurred four and seven months postoperatively. One patient died. The patients had had valve replacement at the same hospital within a few weeks of one another, raising the question of nosocomial acquisition of the organism. The final case was a chronic cutaneous ulcer at the site of an injury that was incurred in a butcher's shop, which may have been the source of the organism.

C bovis grows on standard media but biochemical testing should be carried out using serum- or lipid-supplemented media. Isolates have been variably sensitive to penicillin. All have been sensitive to erythromycin. In one case there was synergy between erythromycin and rifampin.[40]

Probably Endogenously Acquired

Corynebacterium xerosis

C xerosis is a member of the normal flora of the skin and nasopharynx. It was originally felt to be a cause of acute conjunctivitis but this is no longer believed.

In 1977 the cases of 11 patients from whom *C xerosis* was isolated over a two-month period were reported from a surgical intensive care unit (SICU) in California.[44] The patients had severe multisystem disease and most had received broad-spectrum antibiotics. Five patients were infected (four with pneumonia, one with wound infection); six patients were colonized (wounds, sputum). Three patients had bacteremia; two died. All of the organisms were sensitive to penicillin, but none were sensitive to nafcillin and only 68 percent and 53 percent of isolates were sensitive to clindamycin and gentamicin, respectively. Because most of the patients in the SICU had received the latter three antibiotics, the authors suggested that overgrowth and invasion by *C xerosis* occurred following antibiotic pressure in these compromised hosts. The bunching of these cases in time and space suggests that nosocomial spread may have occurred, but the authors felt this unlikely because the antibiograms and biochemicals of the isolates were different.

Two cases of prosthetic valve endocarditis occurring 1 and 14 months postoperatively have also been reported.[45] In one, cultures required 8 to 15 days to become positive. Annular invasion and dehiscence required replacement of the prosthesis in both cases. One patient died of a cerebral embolus. Both patients had received prophylaxis with methicillin and oxacillin. Although in both cases the isolates were sensitive to penicillin, one isolated organism was tolerant (minimal inhibitory concentration [MIC] = 0.17, minimal bactericidal concentration [MBC] = 20 μg per ml).

C xerosis grows well on standard media. All strains reduce nitrate and ferment glucose, fructose, galactose and sucrose. Penicillin or vancomycin, possibly with an aminoglycoside, would seem to be the drugs of choice, but antimicrobial susceptibility testing should guide therapy.

Corynebacterium pseudodiphtheriticum (Corynebacterium hofmannii)

C pseudodiphtheriticum is a normal commensal of the human nasopharynx. Human infections, some poorly characterized, have all been cases of endocarditis on abnormal valves.[4,46] Of seven reported cases three involved prosthetic valves, two occurred in patients with rheumatic valvular disease, one was in a patient with congenital heart disease and one patient had had preceding endocarditis. Interestingly, five of the seven patients had previous or coexistent endocarditis with another organism. Three died—two had prosthetic valve endocarditis and one died in the preantibiotic era.

C pseudodiphtheriticum grows on standard media. The organism reduces nitrate and hydrolyzes urea but is inactive in carbohydrates.

C hemolyticum

C hemolyticum is a commensal of the normal human skin and nasopharynx. Since the initial description by MacLean and associates in 1946[47] of organisms isolated from patients evacuated from the Pacific Islands after World War II, there have been several reports implicating this agent in pharyngitis and cutaneous lesions. Most large series have been from the tropics[48] or England,[49,50] but cases from the United States have been described.[51]

Among 150 cases of *C hemolyticum* pharyngitis from series where age and sex have been delineated, most occurred in older children and young adults (74 percent less than 25 years old) and more often in women and girls (63 percent). The clinical presentation closely mimics streptococcal pharyngitis; follicular tonsillitis, fever, leukocytosis and submandibular adenopathy are common, but a pseudodiphtheritic membrane has also been described.[51] Septicemia has been reported.[52] In reports from England pharyngitis was accompanied by a pruritic maculopapular or scarlatiniform rash over the trunk and extremities in almost 50 percent of cases. Desquamation can occur. Disease in household contacts has been described. In English reports *C hemolyticum* was isolated in pure culture in 130 of 139 cases (94 percent); in the tropics coisolation of other pharyngeal pathogens *(C diphtheriae, Streptococcus pyogenes)* occurred in 35 of 72 patients (49 percent).

Because careful viral and *Mycoplasma* cultures have not been carried out in most of these reports, there remains some doubt about the pathogenicity of *C hemolyticum* in pharyngitis. MacLean and co-workers[47] were unable to produce symptoms by spraying the organisms on the pharynx of volunteers. However, its isolation in pure culture from cases with pharyngitis, disappearance from

the throat coexistent with both antibiotic therapy and symptomatic improvement, the recognition of culture-positive symptomatic recurrences and the demonstration of high titers of specific antibody all suggest that this organism may be a cause of pharyngitis. The disease is likely vastly underreported, as most pharyngeal corynebacteria are not speciated and are disregarded unless a physician suspects *C diphtheriae*.

Approximately 50 cutaneous lesions from which *C hemolyticum* has been isolated have been reported, primarily from the tropics.[47-49] A coexisting pathogen, usually *S pyogenes or Staphylococcus aureus,* has been isolated from 75 percent of the cases, though *C hemolyticum* has shown the most abundant growth. Patients with cutaneous lesions (ulcers, cellulitis) were typically older men. Rash was not described.

Miscellaneous reports include two cases of brain abscess in young boys[53,54] and two cases of osteomyelitis.[47,55]

Like *C pyogenes, C hemolyticum* is catalase negative and β-hemolytic. Growth and hemolysis on sheep blood agar are poor, and human or rabbit blood agar are preferred for isolation. After colonies have been scraped aside with a wire loop, pitting of the underlying agar may be evident; alternatively, the colony may leave a small central dot adherent to the agar. Guidelines for the recognition of *C hemolyticum* have been reported by the CDC.[56]

The organism has been consistently sensitive to penicillin, erythromycin and tetracycline. Recurrences have responded to a second course of antibiotics.

Group JK

Although their ecological niche remains unknown, the group JK diphtheroids are probably normal human commensals. Since their description by Hande and colleagues in 1976,[57] the group JK diphtheroids have emerged as important pathogens in two patient populations: immunocompromised patients and patients with prosthetic heart valves.

More than 100 cases of infections due to group JK in compromised hosts have been reported, generally in men (76 percent) over the age of 16 (95 percent) with hematologic malignancy or undergoing bone marrow transplantation.[57-61] Patients with solid tumors frequently are colonized but infections do not commonly develop.[61] Stamm and co-workers[59] have speculated that the prevalence among older men is due to the higher skin sebum levels (secondary to circulating androgens), which favors the growth of these lipophilic diphtheroids on the skin.

Colonization among 98 oncology patients at two hospitals was 30 percent to 40 percent.[59,60] It has been cultured from 0 percent to 12 percent of normal adults and from 13 percent of patients in an acute care hospital. These values represent low estimates because selective antibiotic media were used for isolation. As it is now known that the resistance of the JK organisms is variable,[9,62] some organisms may have been missed. Colonization was most frequent among older men following a prolonged stay in hospital. Nosocomial acquisition and clustering of cases have been described,[60,61] though up to half of patients in whom colonies have been found may be colonized on admission. Most frequently colonized sites were in the inguinal area (89 percent), rectum (87 percent), axilla (70 percent) and throat (9 percent). Hospital reservoirs apart from colonized patients have not been identified.

Bacteremia, pneumonia and cutaneous infections, particularly at bone marrow biopsy sites, perirectal abscesses, and at hyperalimentation and intravenous catheter sites, were most prevalent. Risk factors for infection included colonization, prolonged granulocytopenia, antibiotic pressure and mucocutaneous defects. Patients with hematologic malignancy or undergoing bone marrow transplantation represented 97 percent of bacteremic patients from four series.[57-59,61]

The organisms produce tiny colonies that may have a metallic sheen after three to four days on blood agar. Biochemical testing may show complete inactivity unless supplemented media and prolonged incubation are used. The CDC have recommended biochemical tests for identification of group JK diphtheroids.[9]

Bacteremic isolates from immunocompromised hosts have been consistently sensitive only to vancomycin. Survival in granulocytopenic patients has been related to use of this antibiotic in addition to replacing intravenous catheters. At the Fred Hutchinson Cancer Research Center in Seattle, the attack rate from 1974 through 1977 ranged from 6 percent to 17 percent of patients per year.[59] At that time a combination of gentamicin, carbenicillin and cephalothin was used as empiric therapy in the febrile neutropenic host. Over the past two years at the same institution there was a single

case of bacteremia due to these organisms. During this period a combination of tobramycin, ticarcillin and vancomycin was used for empiric antibiotic therapy. Inclusion of vancomycin in these patients' initial antibiotic regimen may be preventing overgrowth of these organisms on the skin, from which later invasion may occur.

Group JK diphtheroids are probably the most common cause of "diphtheroid" prosthetic valve endocarditis (PVE). Although many reports described infection undoubtedly due to these organisms,[63-65] incomplete speciation was performed on these isolates. There are 26 confirmed cases[62,66-68]; 18 represent all but one of a series of patients with diphtheroid PVE recently reported from Boston.[62] There were infections of 20 prosthetic valves, 4 valvuloplasties, 1 porcine valve and 1 epicardial pacemaker. All had received perioperative antibiotics, the vast majority to which the organisms were resistant. Patients were older (23 to 65 years) but sex was generally not specified. Most cases occurred within the first 60 days postoperatively (73 percent). Identification of the oganisms required approximately six days; in one case the primary isolation was made after 44 days.

Antimicrobial therapy alone was successful only in the absence of congestive heart failure or a paravalvular leak; the presence of either of these conditions necessitated surgical intervention for survival. Myocardial and annular invasion with valve dehiscence was typically seen. Overall survival was 50 percent and was comparable in the medically and surgically managed groups.

These organisms displayed a variable antibiogram. All isolates were sensitive to vancomycin, and most (82 percent to 86 percent) were sensitive to erythromycin, tetracycline and the aminoglycosides. Over 90 percent were resistant to penicillin and the semisynthetic penicillins. Synergy has been shown between vancomycin or penicillin and gentamicin.[62] The addition of rifampin has been advocated, but sensitivity of group JK organisms to rifampin has been variable. The mechanism by which these organisms are multiply antibiotic-resistant is unknown. Organisms tested do not elaborate β-lactamase and plasmids have not been identified by electron microscopy or agarose gel electrophoresis.

It is possible that these organisms play a role in infections in other patients with implanted devices, particularly those with CSF shunts.[41-43]

TABLE 3.—*Nondiphtheriae Corynebacterial Infections in Humans and Their Pathogens*

Endocarditis
Group JK, *Corynebacterium xerosis, Corynebacterium pseudodiphtheriticum, Corynebacterium bovis, Corynebacterium pyogenes*
Pharyngitis
Corynebacterium hemolyticum, Corynebacterium ulcerans
Cutaneous infections
C hemolyticum, C pyogenes, Group JK, *C bovis*
Lymphadenitis
Corynebacterium ovis
Pneumonia
Corynebacterium equi, Group JK, *C xerosis, C ovis*
Central nervous system infections
C bovis, C hemolyticum
Nephritis
C bovis (cerebrospinal fluid shunt)
Compromised host
Group JK, *C equi, C xerosis*

Miscellaneous Corynebacterial Infections

Rare or poorly characterized infections due to *Corynebacterium aquaticum,*[69] *Corynebacterium genitalium,*[70] *Corynebacterium minutissimum,*[71] *Corynebacterium striatum,*[72] *Corynebacterium enzymicum*[73] and various unclassified corynebacteria[74-76] have been reported, and many others have been referred to the CDC.

Concluding Remarks

Infections caused by the nondiphtherial corynebacteria are summarized in Table 3. It is hoped that these reports will stimulate the speciation of all pathogenic diphtheroids. Only in this manner will distinctive clinical syndromes caused by some of these organisms emerge, and we can thus better understand the proper role of diphtheroids in human disease.

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